

What do Lyme disease and syphilis have in common? Two pathogenic spirochetes unexpectedly share an ATP synthase

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Diseases spread by ticks are not recent phenomena to the New World. However, one tick-borne disease, known in Europe since the beginning of the century, has only recently emerged in the United States and is now the most common tick-borne disease on this side of the Atlantic.

In the mid-1970s, a number of residents of the small town of Lyme in Connecticut were afflicted with an unusual arthritis-like condition. Most new cases were observed in the summer and early fall of each year, and the incidence was soon linked to recent tick bites in a high percentage of patients.

The organism that causes Lyme disease is a bacterium, *Borrelia burgdorferi*, which was cultured from the midgut of *Ixodes* ticks in the mid-1980s. It is shaped like a wave or helix and belongs to a whole class of bacteria that can be identified by this distinctive shape, the spirochetes, which include some other nasty human pathogens that can cause syphilis, tick-borne relapsing fever, dysentery, and leptospirosis.

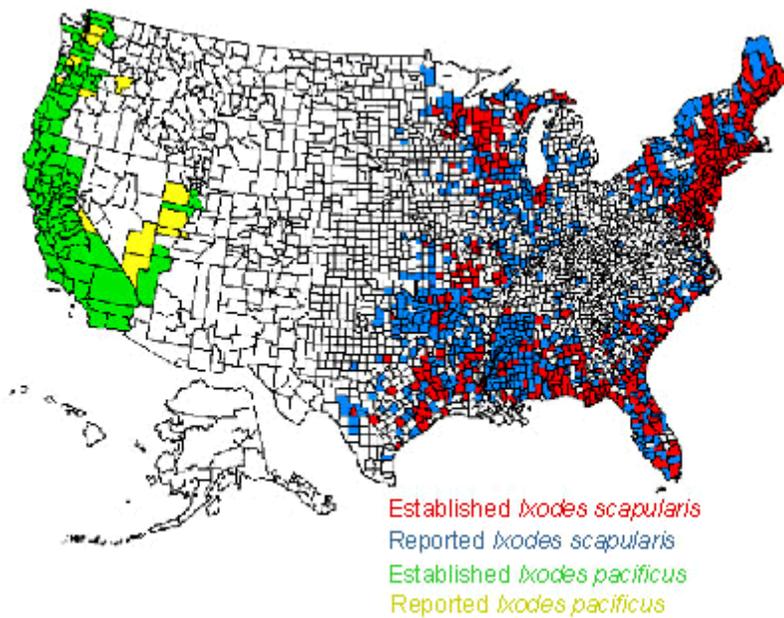
We now have the full sequence of the *B. burgdorferi* genome. It has a total of 853 genes on one linear chromosome and an additional 430 genes on 11 plasmids. The chromosomal genes are required for cell growth, although there are no genes present that are involved in the synthesis of amino acids, fatty acids, enzyme cofactors, or nucleotides. The genes on the plasmids may be involved in infectivity and virulence. One of the chromosomal genes codes for "outer surface protein A" (OspA), which has been the focus of a search for a vaccine against

Lyme disease. Recent clinical trials using a recombinant form of OspA as a vaccine look extremely promising.

But what of the relatives of *B. burgdorferi*? Perhaps one of the most infamous of these is *Treponema pallidum*, the bacterium that causes syphilis. In contrast to Lyme disease, syphilis is not a modern affliction; it was first recognized in the 15th century in Europe. It is similar to *B. burgdorferi* in that it is a spirochete with a relatively small genome and requires a host to survive; however, at the genomic level, the two organisms are not very closely related to each other at all.

Of the 1041 protein-coding regions in *Treponema pallidum*, 476 are shared with *B. burgdorferi*, but nearly half of these are common to other bacteria too, and most have a predicted biological function. Of the genes with unknown function, there are about 50 that are conserved only in the spirochetes and are not found in any other bacteria. Some of these are likely to represent genes that code for spirochete-specific traits, such as their helical shape and perhaps elements of their pathogenicity.

The comparison of whole genomes may help pinpoint genes that make an organism a successful pathogen or suited to living in a particular environment. Furthermore, the identification of related genes in different species gives a new twist to the classification of different organisms, deepening our understanding of their relationship to each other across the whole evolutionary spectrum.



Distribution of Lyme disease vectors in the US The map shows the established and reported distribution of the Lyme disease vectors in the United States, by county, 1907-1996.

'Established' is defined as at least six ticks or two life stages (larvae, nymphs or adults) being identified; 'reported' is defined as at least one tick being identified.

Box: Search PubMed for gene sequencing of Lyme disease

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How is gene sequencing helping us understand Lyme disease? [http://www.ncbi.nlm.nih.gov/Coffeek/CB4_Lyme/PQ1.html]

Box: Search PubMed for Lyme disease and syphilis

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Where do Lyme disease and syphilis converge? [http://www.ncbi.nlm.nih.gov/Coffeek/CB4_Lyme/PQ2.html]

Box: Use BLAST to search for an ATPase found in spirochetes

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An unusual way to generate energy in the spirochetes? [http://www.ncbi.nlm.nih.gov/Coffeek/CB4_Lyme/BQ.html]